

Total fasting, hyperuricaemia and gout

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Summary

Hyperuricaemia occurred in forty-two obese subjects treated by total fasting.

This was apparently harmless in that it did not lead to acute gout in any patient, including one male known to be a sufferer from gout.

The relationship between hyperuricaemia and the acute arthropathy of gout is discussed.

Introduction

The purpose of this communication is to draw attention to the apparently harmless hyperuricaemia which results from treating obese patients by total fasting.

In such patients there is a progressive fall in the glomerular filtration rate during the fasting period resulting in the renal retention of urate (Murphy & Shipman, 1964). In addition there is competition between the ketone bodies and urate for the same, or a similar, renal transport mechanism (Cheifetz, 1965); this also results in the renal retention of urate. The resultant hyperuricaemia is on occasions gross, and has been associated with the acute joint disturbance typical of gout in a significant number of patients in the reported studies of Bloom (1959), Duncan, Frazer & Cristofori (1962) and Drenick *et al.* (1964). Consequently, a history of gout in an obese patient has been accepted as being a strong contraindication to treatment by total fasting. Gilliland (1968) commenced probenecid therapy before the starvation period in patients with gout.

To date, we have studied forty-two obese patients treated by total fasting. The periods of observation ranged from a minimum of 3 weeks to 8 months, in the individual subject. Elevated levels of serum uric acid occurred in all, and in Table 1 the maximum serum uric acid levels are recorded. Despite this none

of the patients, among whom was included a known sufferer from gout, developed any joint upset.

In view of the current attitudes to this problem, a brief case history of the gouty subject is appended.

Case report of J.F.

An obese male patient aged 48 years with a history of gout of 8 years' duration was re-admitted to the ward in relapse. The attack began 2 days prior to admission, with severe pain and swelling of the right knee and subsequent involvement of the metatarso-phalangeal joints of both big toes, the ankles and the left knee. The affected joints were swollen, hot and tender. There was a large, tophaceous deposit on the posterior aspect of the proximal interphalangeal joint of the left third finger. Examination of the other systems was essentially negative, except that the patient gave a history of chest tightness on exertion, relieved by rest. Blood pressure on admission was 180/90 mmHg.

Investigations

Hb 12.6 g/100 ml; WBC 7800/mm³; ESR 78 mm/hr; serum uric acid (on admission) 8.8 mg/100 ml; blood urea and electrolytes, normal; liver function tests, normal; BSP excretion test, 20% and 12% retention of the dye at 30 and 45 min, respectively. The urine was chemically and microscopically normal, except for the expected presence of urate crystals. X-ray of the left hand showed punched-out lesions in the proximal phalanx of the left third finger and narrowing of the proximal interphalangeal joint.

Treatment

The patient was given 0.5 g colchicine once by mouth, in addition to sulphapyrazone (Anturan) 100 mg every 6 hr. The acute joint symptoms subsided rapidly. Five days after admission this therapy was withdrawn.

At this point, because of his obesity and the radiological evidence of widespread joint degeneration, it was decided to treat him with total fasting,

TABLE 1. Maximum serum uric acid values in forty-two fasting, obese subjects (mg/100 ml)

	5-9.9	10-14.9	15-19.9	20+	Data incomplete
Males	2	5	3	2	1
Females	12	9	2	1	5

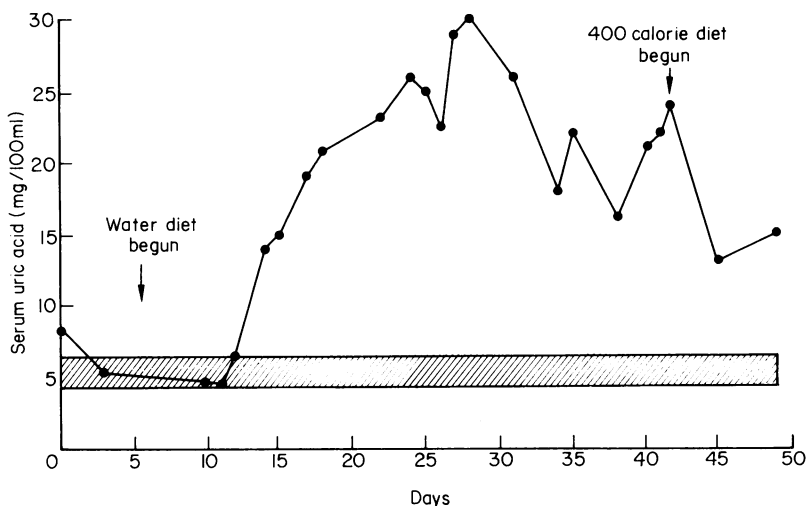


FIG. 1. Serial serum uric acid values in a fasting, gouty subject. Normal range shown by hatched bar.

whilst maintaining a close watch for the earliest symptoms of gout. The possibility of the ensuing hyperuricaemia precipitating an attack of gout was stressed to the patient. He, nevertheless, agreed that all drug therapy should be withheld during this period.

The patient fasted for 34 days. Serial values of the serum uric acid are recorded in Fig. 1. From this, it can be seen that between the 5th and 9th days of fasting the serum uric acid rose from 4 to 15 mg/100 ml and remained above this latter value for a further 28 days. The patient was given a 400 calorie diet and the level of serum uric acid fell from 23.8 to 13 mg/100 ml within 3 days. On discharge it was still elevated at 15 mg/100 ml.

Throughout this period he remained symptom free, losing in the process 23 lb (10.4 kg). On discharge from hospital, an 800 calorie diet was prescribed, and sulphinpyrazone in a dose of 100 mg three times a day.

Discussion

The relationship between hyperuricaemia and acute arthropathy is not a direct one. Asymptomatic hyperuricaemia is common in the relatives of gouty subjects. In sufferers from gout, relapse is associated with a rise in the level of serum uric acid and therapy designed to maintain a normal blood level of uric acid can prevent relapse. The acute joint disturbance typical of gout has been described in other conditions in which the serum uric acid is raised such as in some of the myeloproliferative disorders, in severe chronic renal failure and following prolonged thiazide diuretic therapy.

In this series five of the forty-two subjects fasted for more than 100 days and two of these for more

than 200 days. The resultant hyperuricaemia did not precipitate an acute joint disturbance in any patient. This was the more remarkable in the known gouty subject, whose serum uric acid exceeded 15 mg/100 ml for 28 days, attaining a maximum value of 30 mg/100 ml and who had been initially admitted to the wards in relapse with a serum uric acid of 8.8 mg/100 ml. The immunity of these patients to the harmful effects of hyperuricaemia is obvious but at present inexplicable.

It has been suggested that the acute joint disturbance of gout may be precipitated by rapid fluctuations in the levels of serum urate (MacLachlan & Rodman, 1967). In these fasting obese patients fluctuating hyperuricaemia was invariable but the changes may have occurred too slowly to precipitate an attack; there is usually a sharp rise in serum urate in the first few days of fasting and a rapid fall when the patients are given food. This effect is clearly shown in the gouty subject (Fig. 1).

Other workers (Gordon, Goldberg & Chosy, 1963; Duncan *et al.*, 1963; Drenick *et al.*, 1964) have reported a significant incidence of gout in their fasting, obese patients. The singular absence of such attacks in our patients led us to suggest that this was due to the known rarity of this disorder in the West of Scotland (Thomson, Runcie & Miller, 1966). The results of the present study show that this was an oversimplification. It is apparent that prolonged hyperuricaemia, even in a gouty subject, need not precipitate attacks of gout. This implies that there are factors other than hyperuricaemia which promote this arthropathy. They were not present in our fasting patients, nor were they operative in the gouty subject, throughout his grossly hyperuricaemic phase.

It is apparent that the pathogenesis of the acute arthropathy of gout, or other hyperuricaemic states, is multifactorial. In an acute attack of gout, urate crystals are found within the affected joint. Similarly an attack may be precipitated by intra-articular injection of suitably prepared monosodium urate crystals (Seegmuller & Howell, 1962). The importance of purely local factors in the genesis of an acute attack is demonstrated by the liability of local joint damage, e.g. direct trauma, exposure to cold, to cause an acute flare-up in the affected part in susceptible persons. The development of the acute attack is related to those factors, acting either systemically or locally, which promote the intra-articular deposition of urate crystals. Some of these are known, for example, trauma. Others are not. The distribution of these attacks involving as they do the metatarso-phalangeal joint of the big toes leads one to speculate that the reason for this is mechanical. While walking the weight of the body is borne along the medial borders of the feet and the metatarso-phalangeal joint becomes the centre of a system at which great mechanical force is exerted. We would, therefore, suggest that this repetitive stress may determine the localization of acute gouty arthropathy by promoting the deposition of urate crystals in these joints.

The harmless nature of the hyperuricaemia accompanying fasting in obese patients is apparent from this study. Furthermore, an obese gouty subject did not relapse while fasting. The reasons for this remain

obscure and further research is required into those factors, other than hyperuricaemia, which lead to the deposition of urate crystals in joints.

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